Carboxyhaemoglobin concentrations were used to assess compliance. Only patients in whom the concentrations fell to under 2% during the no-smoking period were included in the study. Concentrations of up to 2% during no-smoking periods are acceptable: non-smokers living and working in the City of London have a mean concentration of 1.3%.¹² During the smoking periods our patients had carboxyhaemoglobin concentrations in excess of 4%.

This study has shown that smoking in addition to its known epidemiological associations has direct and adverse effects on the heart. These were still evident after treatment with propranolol and represent a hindrance to the effective medical treatment of angina pectoris.

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References

- Oram S, Sowton E. Tobacco angina. *Q J Med* 1963;32:115-43.
- McHenry PL, Farris JV, Jordan JW, Morris SN. Comparative study of cardiovascular function and ventricular premature complexes in smokers and non-smokers during maximal treadmill exercise. *Am J Cardiol* 1977; 39:493-8.
- Aronow WS, Cassidy J, Vangrow JS, *et al.* The effect of cigarette smoking and breathing carbon monoxide on cardiovascular hemodynamics in anginal patients: *Circulation* 1974;50:340-7.
- Aronow WS, Kaplan MA, Jacob D. Tobacco: a precipitating factor in angina. *Ann Intern Med* 1968;69:529-36.
- Fox K, Selwyn A, Shillingford J. Precordial exercise mapping: improved diagnosis of coronary artery disease. *Br Med J* 1978;ii:1956-8.
- Fox KM, Selwyn AP, Shillingford JP. A method for precordial surface mapping of the exercise electrocardiogram. *Br Heart J* 1978;40:1339-43.
- Mason RE, Likar I, Biern RO, Ross RS. Multiple lead exercise electrocardiography. Experience in 107 normal subjects and 67 patients with angina pectoris and comparison with coronary cinearteriography in 84 patients. *Circulation* 1967;36:517-25.
- Aronow WS, Rokaw SN. Carboxyhaemoglobin caused by smoking non-nicotine cigarettes: effects in angina pectoris. *Circulation* 1971;44: 782-8.
- Routledge PA, Shand DG. Clinical pharmacokinetics of propranolol. *Clin Pharmacokinet* 1979;4:73-90.
- Wood AJJ, Vestal RE, Branch RA, Wilkinson GR, Shand DG. Age related effects of smoking on elimination of propranolol, antipyrine and indocyanine green. *Clinical Research* 1978;26:297A.
- Walle T, Conradi EC, Walle UK, Fagan TC, Gaffney TE. The predictable relationship between plasma levels and dose and chronic propranolol therapy. *Clin Pharmacol Ther* 1978;24:668-77.
- Castleden CM, Cole PV. Carboxyhaemoglobin levels of smokers and non-smokers working in the City of London. *Br J Ind Med* 1975;32:115-8.

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SHORT REPORTS

Programme to encourage self-examination for breast cancer

Four years ago I reported¹ the preliminary results of a study designed to discover whether women could be persuaded to examine their breasts regularly and, if so, whether regular self-examination increased the rate of diagnosis of early breast cancer. Two women's organisations in Finland co-operated and 56 000 of their members aged 20 to 80 years enrolled in the study. Person-to-person education and instruction were arranged and these were supplemented by mass communication through television, radio, and the press. Surgeons and radiologists in different parts of Finland agreed to see women who had detected signs by self-examination. The results of the combination of mass health education and personal instruction were encouraging and after two years about 70% of the women were persisting with regular self-examination.

Since then there has been a continuing national educational programme, the "Mama Programme," and I report a study of its results.

Subjects, methods, and results

The population studied consisted of 56 177 women aged 20 years or over in the whole of Finland. The Mama Programme consists of person-to-person instruction, follow-up inquiry into persistence of self-examination and the results of it, television education, and the provision of medical specialists whom women who detect signs may consult.

Before the start of the programme all of a group of 4000 women interviewed knew of the need for monthly self-examination of the breasts but only 2% of them practised it regularly. Since the start of the programme almost 67% of 2900 women in one area have examined themselves regularly each month.

In the first year of the programme 750 of the 56 177 women consulted a medical specialist. One out of every eight of them had a new breast cancer and 90 self-detected new cases were registered. In the second year about 300 consulted a specialist and 35 self-detected new cancers were registered. The 90 new self-detected cases in the first year was almost double the figure expected from the incidence recorded in Finland for the previous year. Cases of local carcinoma numbered 63 (70%) and the mean age of the patients was about 10 years younger than expected. Cases of duct carcinoma were about double the expected number. Cases of carcinoma with axillary spread numbered 27, compared with the 39-55 that could have been expected from the Finnish Cancer Register. The mortality expected for a group similar to that in the study was 28-75, but in fact only 15 of the new cases detected in the programme died.

A sharp rise in the incidence of breast cancer in Finland during 1973-80 was not predicted. In 1972, the year before the start of the Mama Pro-

gramme, there were 1126 new cases of breast cancer. In 1973 there were 1301 cases and in 1976 1406. Since 1975 the Mama Programme has been introduced to about 100 000 more women each year, and it is recommended by health authorities. The number of registered cases of breast cancer has risen sharply since the programme was introduced.

Comment

The results show that the programme has greatly reduced the mortality in new breast cancer cases. The incidence of breast cancer in Finland is low. In countries where it is high a long-term educational programme of this kind could be of great value. Breast cancer screening cannot be arranged for all women—at all events, not often enough. A programme of self-examination is not hindered by numbers and is effective.

- G Gästrin. New technique for increasing the efficiency of self-examination in early diagnosis of breast cancer. *Br Med J* 1976;iii:745-6.

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Suspected chloroquine-resistant malaria in Nigeria

The emergence of chloroquine-resistant malaria, first reported from South America and South-East Asia, has been suspected in Africa since 1965. Olatunde¹ described seven cases of resistance suspected on clinical grounds, all from southern Nigeria, while Khan and Maguire,² and Fogh, Jepsen, and Effersøe³ studied in detail individual cases originating from Zambia and Kenya respectively. The Kenya case was claimed to be the first confirmed case from that country that met the World Health Organisation's criteria of resistance. Suspicion is growing in northern Nigeria that chloroquine is becoming less certainly effective in treating malaria, and our suspicion is based on cases like the following.

Case report

A 28-year-old European woman presented with nausea and mild diarrhoea. She was taking pyrimethamine 25 mg twice weekly for malaria prophylaxis. A blood film showed malaria parasites. Unfortunately facilities were not available for species identification, but the malaria in the district was generally assumed to be due to *Plasmodium falciparum*. She was given a course of chloroquine by mouth to a total of 1800 mg. For a body weight of 45 kg that amply met the WHO recommended standards. She had no diarrhoea or vomiting while taking the drug. She had never had malaria before nor had she previously taken chloroquine. The treatment did not relieve her symptoms—in fact, they were added to by the drug's side effects. Five days after her initial presentation a blood film, examined at a different laboratory, showed abundant parasites. Her haemoglobin concentration was 12 g/dl. She was therefore given Fansidar (pyrimethamine 25 mg, sulphadoxine 500 mg) three tablets immediately.

Four days later she again attended, feeling weak and dizzy, with a temperature of 38°C. There were still a few plasmodia in the blood film. She was given chloroquine 800 mg immediately, to be repeated once weekly for three weeks—although only one of these doses was taken. She slowly improved, and two weeks after her first attendance her blood film was clear. No parasites were found in a repeat film after a further two weeks.

Comment

While we have no absolute proof of the existence of chloroquine-resistant malaria in our part of Africa we strongly suspect it because of several cases like this one, mostly in Africans. I have chosen to report this case because it is well documented although it is atypical in that the patient was a European taking regular prophylaxis. I am sure I am by no means alone in believing that resistance of *P falciparum* to chloroquine exists in Africa and that our regimens of treatment and chemoprophylaxis therefore need to be reconsidered.

¹ Olatunde A. Chloroquine-resistant *P falciparum* and malaria in Africa. *Trans R Soc Trop Med Hyg* 1977;71:80-1.

² Khan AA, Maguire MJ. Relative chloroquine resistance of *P falciparum* in Zambia. *Br Med J* 1978;ii:1669-70.

³ Fogh S, Jepsen S, Effersøe P. Chloroquine-resistant *P falciparum* malaria in Kenya. *Trans R Soc Trop Med Hyg* 1979;73:228-9.

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Captopril-induced pemphigus

Captopril (SQ 14225), an oral inhibitor of angiotensin-converting enzyme, offers a new approach to treating several forms of hypertension. The commonest unwanted effects are morbilliform or maculopapular rashes and fever, which usually resolve on stopping or reducing the dose.¹ Other unwanted effects include aphthous ulcers of the mouth, temporary ageusia, the nephrotic syndrome, and reversible renal failure.¹ We report a case of pemphigus induced by captopril.

Case report

A 45-year-old previously fit English Jew began captopril 25 mg thrice daily in July 1979 for essential hypertension. The dose was increased weekly for four weeks to 150 mg thrice daily. Propranolol 10 mg thrice daily was added, being increased at weekly intervals until control was achieved with 80 mg thrice daily. He remained on the same dose of both drugs until January, when he presented with a two-week history of lesions on the trunk, scalp, and face and painful tongue erosions. The skin lesions were sore, red patches which had rapidly lost their surface, oozed, and crusted. Pemphigus erythematosus was diagnosed. Captopril was stopped, and after five weeks the skin and mouth ulcers had healed, though one new cutaneous lesion appeared. Blood cell count, erythrocyte sedimentation rate, blood glucose concentrations, liver and renal function values, protein electrophoresis, and immunoglobulin and serum complement concentrations were normal; antinuclear factor was speckled positive at 1/10.

Autoantibody to epidermal intercellular cement substance was positive at 1/40. Skin biopsy of the trunk showed an intraepithelial bulla high in the epidermis, containing a few acantholytic cells. On direct immunofluorescence upper epidermal intercellular IgG and lower epidermal intercellular C3 were detected in a biopsy specimen of a lesion. There was basement-membrane

deposition of C3 in perilesional skin. These appearances were consistent with pemphigus erythematosus. The HLA genotype was HLA-A1, 3/8, 18/BL, -1/6/DRW3, DRW5.

Comment

Though several hundred patients have been treated with captopril for at least six months, this is the first report of captopril-induced pemphigus. In Jewish patients with pemphigus vulgaris there is a particularly high prevalence of HLA-A10 and DRW4.² Our patient had neither of these.

Chemical structures of captopril and penicillamine.

The chemical structures of penicillamine and captopril are strikingly similar (figure). Each compound has a highly reactive, negatively charged sulphhydryl group in a stable stereochemical relation to a similarly negatively polarised oxo group. The stereochemical similarities between penicillamine and captopril, combined with the clinical evidence of their ability to produce similar disorders, suggest that the toxicity of both drugs may prove disconcertingly similar.

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¹ Atkinson AB, Robertson JIS. Captopril in the treatment of clinical hypertension and cardiac failure. *Lancet* 1979;ii:836-9.

² Park MS, Terasaki PI, Ahmed AR, Tiwari JL. HLA-DRW4 in 91% of Jewish pemphigus vulgaris patients. *Lancet* 1979;ii:441-2.

³ Marsden RA, Ryan TJ, Vanhagen RI, Walshe M, Hill H, Mowat AG. Pemphigus foliaceus induced by penicillamine. *Br Med J* 1976;iv:1423-4.

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Systemic lupus erythematosus and nephritis: severe relapse with disappearance of antinuclear antibodies

Exacerbations of systemic lupus erythematosus with active renal disease are almost always associated with high plasma titres of antinuclear factor (ANF) and DNA-binding antibody (anti-ds DNA).¹ We describe a patient with classical systemic lupus erythematosus and initial high titres of antinuclear antibodies in whom severe relapse resulting in renal failure coincided with a prolonged reversion to normal of these serological indices.

Case report

A 20-year-old woman developed the nephrotic syndrome and a butterfly rash. Results of investigations were: haemoglobin concentration 9.6 g/dl; platelet count $87 \times 10^9/l$ ($87\,000/mm^3$); serum electrolyte, urea, and creatinine